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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,139	07/31/2003	Stevan R. Hubbard	1049-1-030N	1823

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EXAMINER	
DEJONG, ERIC S	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,139	HUBBARD ET AL.	
	Examiner	Art Unit	
	Eric S. DeJong	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *7,17 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-16,18-25 and 27-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/11/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Election/Restrictions

Applicant's election of Species A (claims 3, 5, 14, 15, 23, and 24), drawn to the three dimensional structure of the tyrosine binding domain of the IGF1 receptor described by the coordinates of Appendix A, in the reply filed on 05/11/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 7, 17, and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 05/11/2006.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/400,001, fails to provide adequate support or enablement in the manner provided by the first paragraph

of 35 U.S.C. 112 for one or more claims of this application. Instant claims 3, 5, 14, 15, 23, and 24 are each drawn to a three-dimensional structure that is the tyrosine kinase domain of the IGF1 receptor described by the coordinates of APPENDIX A. However, upon review, neither APPENDIX A nor three-dimensional coordinates of any portion of IGF1 receptor have been disclosed in provisional Application No. 60/400,001. It is acknowledged that page 1 of said provisional application contains a reference to a Microfiche Appendix in paragraph 0001 and further that claims 4, 6, 11, and 15 of the provisional application each recite limitations drawn to "the coordinates of APPENDIX A", however said provisional application does not actually provide or disclose a set of coordinates on a microfiche appendix nor an Appendix A. is not a sufficient of actual disclosure of said coordinates. Since applicants have provided in the instant application a set of coordinates for a structure of IGF1 in APPENDIX A, claims 3, 5, 14, 15, 23, and 24 are given priority to the effective filing data of the instant application, received on 31 July 2003. Sufficient support has been found for instant claims 1, 2, 4, 6, 8-13, 16, 18-22, 25, and 27-32 in said provisional application, therefore claims 1, 2, 4, 6, 8-13, 16, 18-22, 25, and 27-32 are given priority to the filing date of said provisional application, received on 31 July 2002.

Information Disclosure Statement

The information disclosure statement filed 05/11/2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the publications listed in said information disclosure statement are not identified by title (see 37 CFR § 1.98(b)(5)). It

has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Drawings

The drawings filed by applicants on 07/31/2003 are objected to for the following reasons:

Figures 1-6 are color drawings. Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> **The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.**

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

In the instant case, applicants have supplied 3 sets of colored drawing. However applicants have not submitted a petition filed under 37 CFR 1.84(a)(2) requesting the

acceptance of colored drawings, paid the appropriate fee set forth in 37 CFR 1.17(h), nor amended the first paragraph of the brief description of the drawings section of the specification as required.

Specification

The disclosure is objected to under 37 CFR § 1.96 for the following reasons: The appendix to the specification, Appendix A filed by applicants on 07/31/2003, lists over 300 lines of computer code that is equivalent to a .PDF computer file format. As such, Appendix A is treated as computer program listing as indicated by 37 CFR § 1.96(a). Regarding material that will be printed in a patent, 37 CFR 1.96(b) states:

> "If the computer program listing is contained in 300 lines or fewer, with each line of 72 characters or fewer, it may be submitted either as drawings or as part of the specification."

Since the Appendix A is over 300 lines in length, said appendix will not be printed as part of a patent that may issue from the instant application.

In regards to an appendix which will not be printed, 37 CFR § 1.96(c) states:

> "Any computer program listing may, and any computer program listing having over 300 lines (up to 72 characters per line) must, be submitted on a compact disc in compliance with § 1.52(e). A compact disc containing such a computer program listing is to be referred to as a "computer program listing appendix." The "computer program listing appendix" will not be part of the printed patent. The specification must include a reference to the "computer program listing appendix" at the location indicated in § 1.77(b)(5)."

Therefore, applicants are required to submit a computer program listing appendix in compliance 37 § 1.52(e) consisting of the listing in Appendix A as required under 37 CFR §1.96.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 8-16, 18-25, and 27-32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-6, 8-16, 18-25, and 27-32 are drawn to methods of for selecting a compound capable of binding to a tyrosine kinase domain of an insulin-like growth factor-1 (IGF1) receptor . A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims are open to embodiments wherein all recited method steps are performed *in silico*. Therefore the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be

"tangible," the process must produce a real world result . Furthermore, the claim must be limited only to statutory embodiments. Thus, if a claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

Claims 1-6, 8-16, 18-25, and 27-32 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. In the instant claims, recited steps drawn to determining if a test compound fits into a three-dimensional structure, selecting a test compound, generating a test compound, contacting a test molecule with a three-dimensional IGF-1 receptor structure, and determining if the test compound binds may all be performed *in silico* using only virtual ligand docking and screening techniques without any requirement of a step for outputting a result to a display or a readily accessible memory. Further the claims do not require a physical transformation step, such as the actual synthesis of a compound or subsequent empirical testing of a result obtained by computational modeling. Therefore, the instant claims do not produce a tangible result.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 13, 18-22, and 27-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Blume et al.

The instant claims are drawn to methods for selecting a compound capable of binding to a tyrosine kinase domain of an insulin-like growth factor-1 receptor comprising determining an ability of a test compound to fit into a three-dimensional structure formed by the tyrosine kinase domain of an insulin-like growth factor-1 receptor, selecting a test compound predicted to fit said structure, generating the test compound, contacting the test compound with said structure, and determining if the test compound binds. Further embodiments include additional steps of determining an ability of a test compound to bind to the insulin receptor and selecting compounds not capable of binding to the insulin receptor.

Blume et al. set forth methodologies of drug discovery and phenomics by use of a process (Diogenesis) wherein surrogate peptide are made, isolated, characterized and utilized for partner identification, target regulation, and small molecule discovery (see Blume et al., Abstract and page 348, col. 1, line 45 through col. 2, line 36). The Diogenesis methodology relies upon synthesizing and screening a diverse library of surrogate peptide molecules which are tested for binding against a target molecule (see also Blume et al., page 351, col. 1, line 8-42). Rare and unique binders are selected that are correlated with surface "hot spots" on the target molecule (see also Blume et al., page 351, col. 1, line 43 through col. 2, line 54). Blume et al. further disclose the example application of the Diogenesis methodology in determining agonists and antagonist surrogate peptides binding to the insulin-Like growth factor receptor (IGF-1R) (see Blume et al., Figures 2 and 3 and page 352, col. 1, line 1 through page 353, col. 2, line 28). In this example of applying the Diogenesis methodology, Blume et al. discloses

the both use and consideration of known three-dimensional structures of IGF-1R, which encompasses the tyrosine kinase domain (IGF1RK, as recited in claims 13 and 22), as well as consideration of the homologous insulin receptor structure (see especially, page 352, col. 1, lines 1-27). Figure 3 of Blume et al. displays the agonist (enhancing activity) and antagonist (reducing activity) of identified surrogate peptides produced by the Diogenesis method performed on IGF-1R.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 3, 5, 14, 15, 23, and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blume et al. as applied to claims 1, 2, 4, 13, 18-22, and 27-32 above, and further in view of Favelyukis et al.

The instant claims are drawn to methods for selecting a compound capable of binding to a tyrosine kinase domain of an insulin-like growth factor-1 receptor, as discussed above, further requiring the use of the tyrosine kinase domain of the IGF1 receptor described by the coordinates of Appendix A.

As discussed above, Blume et al. set forth methodologies of drug discovery and phenomics by use of a process (Diogenesis) wherein surrogate peptide are made, isolated, characterized and utilized for partner identification, target regulation, and small

molecule discovery. While Blume et al. does teach the use of three-dimensional structure coordinates in the disclosed Diogenesis methodology, Blume et al. does not fairly teach or suggest the use of the structure coordinates of Appendix A.

Favelyukis et al. disclose the determination and deposition of three dimensional structure coordinates encompassing the tyrosine kinase domain of the IGF1 receptor (Protein Data Bank, accession code 1K3A, see Favelyukis et al. page 1063, col. 1, lines 9 and 10). It is acknowledged that the inventive entity for the instant application is identical to the authors of the Favelyukis et al. reference. However, since claims 3, 5, 14, 15, 23, and 24 are given priority to the effective filing date of the instant application (31 July 2003), the reference of Favelyukis et al. published December 2001 qualifies as prior art against the instant claims. It is further noted that since claims 1, 2, 4, 13, 18-22, and 27-32 are given priority to the provisional application 60/400,001 (filed 31 July 2002), said claims are not included under this rejection.

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use the three dimensional structure coordinates encompassing the tyrosine kinase domain of the IGF1 receptor in with the Diogenesis methodology disclosed by Blume et al. because Blume et al. sets forth the use of available three-dimensional structure coordinated of the IGF-1 receptor (see especially, page 352, col. 1, lines 1-27).

Claims 1, 2, 4, 6, 8-11, 13, 16, 18-22, 25, and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blume et al. as applied to claims 1, 2, 4, 13, 18-22, and 27-32 above, and further in view of Hou et al.

The instant claims are drawn to methods for selecting a compound capable of binding to a tyrosine kinase domain of an insulin-like growth factor-1 receptor, as discussed above, wherein the computer-assisted method comprises virtual ligand docking and screening techniques capable of designing and or/ identifying a compound predicted to bind a three-dimensional motif of the tyrosine kinase domain of the IGF1 receptor.

As discussed above, Blume et al. set forth methodologies of drug discovery and phenomics by use of a process (Diogenesis) wherein surrogate peptide are made, isolated, characterized and utilized for partner identification, target regulation, and small molecule discovery. While Blume et al. does teach the use of three-dimensional structure coordinates in the disclosed Diogenesis methodology, Blume et al. does not fairly teach or suggest the use of virtual ligand docking and screening techniques capable of designing and or/ identifying a compound.

Hou et al. set forth computational methods for modeling the docking of protein-protein and protein-peptide interactions (see Hou et al., Abstract). Hou et al. further disclose that such molecular docking procedures have been very effective in the study of protein ligand interactions, and the structural information from the theoretically modeled complex may help clarify the mechanisms behind molecular recognition and may be used in ligand design (see Hou et al., page 639, col. 2, lines 1-9).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use the computational docking procedures, as taught by Hou et al., with the Diogenesis methodology, as taught by Blume et al., because Hou et al. teaches that computational modeling is useful for studying peptide-protein interactions as well as ligand design.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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